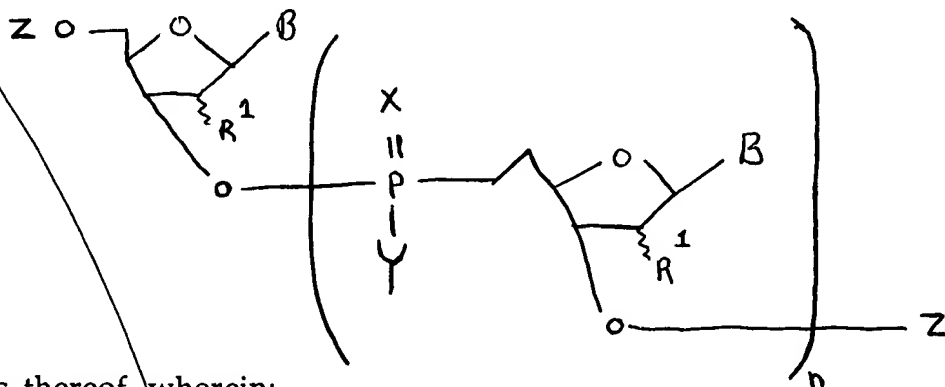


What is claimed is:

- Add
D'
1. A modified oligonucleotide or derivative thereof, as herein defined, wherein the modification comprises substitution, for one or more linkages between individual nucleotide residues which are synthesized utilizing phosphotriester solid phase synthesis chemistry, of a methylene phosphonate type linkage of the formula (I):



and stereoisomers thereof, wherein:

- each B is independently a purine or pyrimidine base or modified form;
each Z is independently a noninterfering substituent, preferably hydrogen, PO_3^- or a protecting group;
each R^1 is independently hydrogen, hydroxyl, fluorine or methyl ester;
each Y is independently OR^2 , $\text{N}(\text{R}^2)_2$ or SR^2 wherein,
each R^2 is independently hydrogen or alkyl (1 - 12 C);
X is selected from oxygen and sulfur;
n is an integer from 1 to 200.

2. The modified oligonucleotide of claim 1 which is a dimer, trimer or tetramer.

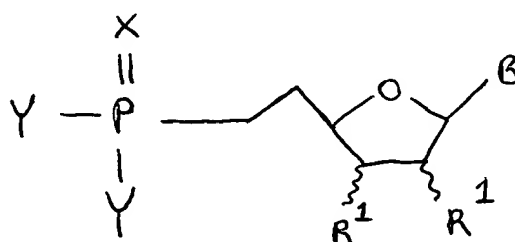
3. The modified oligonucleotide of claim 1 comprising
a first nucleotide sequence containing at least three nucleotide residues,
said sequence having either 3' to 5' or 5' to 3' polarity, and, coupled thereto,
a second nucleotide sequence containing at least one nucleotide
residue, said second sequence having polarity inverted from that of the first
sequence.

4. The oligonucleotide of claim 3 which is capable of forming a triplex with a target duplex DNA.

5 5. The oligonucleotide of claim 4 which is capable of forming a covalent crosslink with a target duplex DNA.

6. The modified oligonucleotide of claim 1 wherein R^1 and R^2 are both fluorine.

10 7. A compound of formula (II):



and stereoisomers thereof, wherein:

B is a purine or pyrimidine base or modified form;

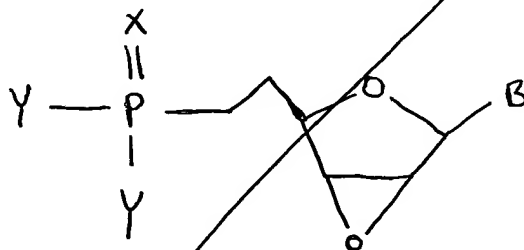
each R^1 is independently hydrogen, hydroxyl, fluorine or methyl ester;

each Y is independently OR^2 , $N(R^2)_2$ or SR^2 wherein,

each R^2 is independently hydrogen or alkyl (1 - 12 C); and

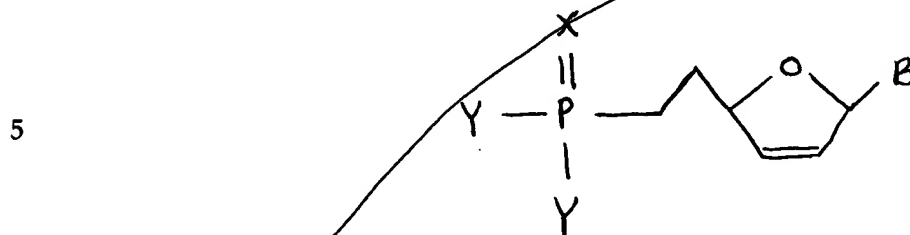
X is selected from oxygen and sulfur.

25 8. A compound of formula (III):



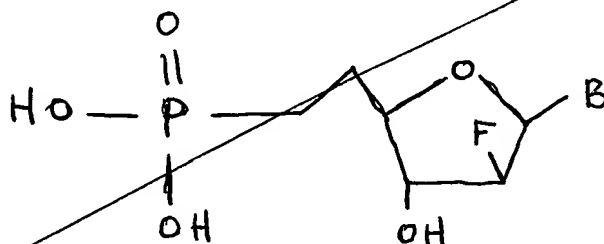
and stereoisomers thereof, wherein B, R^1 , R^2 , Y and X have any of the meanings given in claim 7.

9. A compound of formula (IV):



10 and stereoisomers thereof wherein B, R¹, R², Y and X have any of the meanings given in claim 7.

Sub B2
10. The compound of claim 7 having the formula (V):



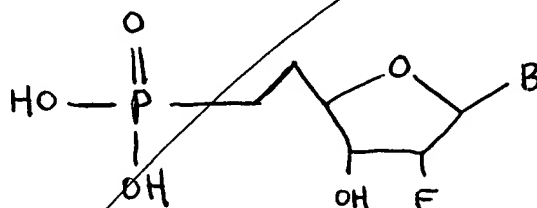
20 wherein B is guanine.

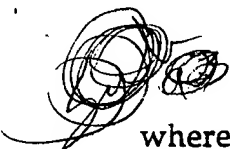
11. The compound of claim 10 wherein B is adenine.

25 12. The compound of claim 10 wherein B is cytosine.

Sub B2
13. The compound of claim 10 wherein B is aziridinylcytosine.

30 14. The compound of claim 7 having the formula (VI):



 wherein B is guanine.

15. The compound of claim 14 wherein B is adenine.

5 16. The compound of claim 14 wherein B is cytosine.

Sub
(3) ~~17. The compound of claim 14 wherein B is aziridinyleytosine.~~

18. The compound of claim 14 wherein B is thymine.

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- 5 19. A pharmaceutical composition useful for treatment of a viral infection or malignant condition which comprises an effective amount of a compound of claim 1 in combination with a pharmaceutically acceptable carrier.
- Sub C4*
B1 20. A pharmaceutical composition useful for treatment of a viral infection or malignant condition which
10 ~~comprises an effective amount of a compound of claim 7 in combination with a pharmaceutically acceptable carrier.~~
- 15 21. The composition of claim 19 in unit dosage form.
22. The composition of claim 20 in unit dosage form.
- 20 23. A method for treatment of viral infection or malignant condition which comprises administering to an individual in need of such treatment an effective amount of a compound of claim 1.
- 25 24. A method for treatment of viral infection or malignant condition which comprises administering to an individual in need of such treatment an effective amount of a compound of claim 7.
- 30 25. The oligonucleotide of claim 1 which is nuclease stable by having 2 or more 5' methylene phosphonate linkages at both 5' and 3' terminal internucleotide residues.
- 35 26. The modified oligonucleotide of claim 1 wherein each B is independently selected from adenine, guanine, cytosine, 5-methylcytosine, aziridinylcytosine, 8-

hydroxy-N⁶-methyladenine, thymine, uracil,
pseudoisocytosine and inosine.

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add
a5
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add
K37

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